

*Amendments to the Claims*

This listing of claims will replace all prior versions, and listings of claims in the application.

1. (Currently Amended) A multiple inducible gene regulation system consisting of two orthogonal gene regulation systems, wherein[:]

[[a)]] each of said orthogonal gene regulation systems comprises:

i) a first polynucleotide encoding a ~~receptor complex~~ a first polypeptide comprising:

A) a DNA binding domain, and [[:]]

B) an ecdysone receptor ligand binding domain; and [[:]]

ii) a second polynucleotide encoding a second polypeptide comprising:

C) a nuclear receptor ligand binding domain capable of forming a dimer with the ecdysone receptor ligand binding domain of said first polypeptide, [[:]] and

D) a transactivation domain; and

iii) [[:]] a third polynucleotide ~~comprising a DNA sequence~~ encoding a third polypeptide, wherein said third polynucleotide is operatively linked to a response element,

wherein binding of the DNA binding domain of said first polypeptide to the said response element results in expression of the said third polypeptide.

2. (Canceled)

3. (Currently Amended) A virus comprising the multiple inducible gene regulation system of claim 1.

4. (Currently Amended) An isolated host cell comprising the multiple inducible gene regulation system of claim 1.

5. -- 8. (Canceled)

9. (Currently Amended) A multiple inducible gene regulation system consisting of two orthogonal gene regulation systems wherein[[:]]

[[a)]] each of said gene regulation systems comprises:

i) ~~a receptor complex~~ a first polypeptide comprising:

A) a DNA binding domain, and [[:]]

B) an ecdysone receptor ligand binding domain; and

ii) a second polypeptide comprising:

C) a nuclear receptor ligand binding domain capable of forming a dimer with the ecdysone receptor ligand binding domain of said first polypeptide, [[:]]

and

D) a transactivation domain; and

iii) [[ii)]] a polynucleotide comprising[[:]]

an exogenous or endogenous gene and a response element[[:]]

wherein[[:]]

[[A]]) the said exogenous or endogenous gene is under the control of the said response element[[[:]] and, wherein  
[[B]]) binding of the DNA binding domain of said first polypeptide to the said response element in the presence of a ligand results in ~~activation of the~~ expression of said exogenous or endogenous gene.

10. (Canceled)

11. (Canceled)

12. (Currently Amended) An isolated host cell comprising the multiple inducible gene regulation system of claim 9.

13. - 49. (Canceled)

50. (Previously Presented) A vector comprising the multiple inducible gene regulation system of claim 1.

51. (Previously Presented) The isolated host cell of claim 4, wherein the host cell is a bacterial cell, a fungal cell, a yeast cell, a plant cell, an animal cell, a mammalian cell, a mouse cell, or a human cell.

52. (Previously Presented) The isolated host cell of claim 51, wherein the host cell is a human cell.

53. (Previously Presented) The isolated host cell of claim 12, wherein the host cell is a bacterial cell, a **fungal** cell, a yeast cell, a plant cell, an animal cell, a mammalian cell, a mouse cell, or a human cell.

54. (Previously Presented) The isolated host cell of claim 53, wherein the host cell is a human cell.

55. (Previously Presented) The multiple inducible gene modulation system of claim 1, wherein **said nuclear receptor ligand binding domain** is selected from the group consisting of a **vertebrate retinoid X receptor ligand binding domain**; an invertebrate retinoid X receptor ligand binding domain; an **ultraspiracle protein ligand binding domain**; and a chimeric ligand binding domain comprising two polypeptide fragments, wherein the first polypeptide fragment is from a vertebrate retinoid X receptor ligand binding domain, an **invertebrate retinoid X receptor ligand binding domain**, or an ultraspiracle protein ligand binding domain, and the second polypeptide fragment is from a different vertebrate retinoid X receptor ligand binding domain, invertebrate **retinoid X receptor ligand binding domain**, or an ultraspiracle protein ligand binding domain.

56. (Currently Amended) The multiple inducible gene modulation system of claim 1, wherein said ecdysone receptor ligand binding domain is selected from the group consisting of a Lepidopteran ecdysone receptor ligand binding domain, a Dipteran ecdysone receptor ligand binding domain, an Arthropod ecdysone receptor ligand binding domain, an Orthopteran ecdysone receptor ligand binding domain, a Homopteran ecdysone receptor ligand binding domain, a Hemipteran ecdysone receptor ligand binding domain, a spruce budworm *Choristoneura fumiferana* ecdysone receptor ligand binding domain, a yellow meal worm *Tenebrio molitor* ecdysone receptor ligand binding domain, a tobacco hornworm *Manduca sexta* ecdysone receptor ligand binding domain, a tobacco budworm *Heliothis virescens* ecdysone receptor ligand binding domain, a golmidge *Chironomus tentans* ecdysone receptor ligand binding domain, a silkworm *Bombyx mori* ecdysone receptor ligand binding domain, a squinting bush brown *Bicyclus anynana* ecdysone receptor ligand binding domain, a buckeye *Junonia coenia* ecdysone receptor ligand binding domain, a fruit fly *Drosophila melanogaster* ecdysone receptor ligand binding domain, a yellow fever mosquito *Aedes aegypti* ecdysone receptor ligand binding domain, a blowfly *Lucilia capitata* ecdysone receptor ligand binding domain, a sheep blowfly *Lucilia cuprina* ecdysone receptor ligand binding domain, a blowfly *Calliphora vicina* ecdysone receptor ligand binding domain, a Mediterranean fruit fly *Ceratitis capitata* ecdysone receptor ligand binding domain, a locust *Locusta migratoria* ecdysone receptor ligand binding domain, an aphid *Myzus persicae* ecdysone receptor ligand binding domain, a fiddler crab *Celuca pugilator* ecdysone receptor ligand binding domain, an ixodid tick *Amblyonima americanum*

ecdysone receptor ligand binding domain, and a white fly *Bamecia argentifoli* ecdysone receptor ligand binding domain.

57. (Currently Amended) The multiple inducible gene modulation system of claim 56 22, wherein said ecdysone receptor ligand binding domain is a spruce budworm *Choristoneura fumiferana* ecdysone receptor ligand binding domain.

58. (Currently Amended) The multiple inducible gene modulation system of claim 1, wherein said DNA binding domain is selected from the group consisting of a GAL4 DNA binding domain, a LexA DNA binding domain, a transcription factor DNA binding domain, a Group H nuclear receptor member DNA binding domain, a steroid/thyroid hormone nuclear receptor superfamily member DNA binding domain, a bacterial LacZ DNA binding domain, a DNA binding domain, and an ecdysone receptor DNA binding domain.

59. (Currently Amended) The multiple inducible gene modulation system of claim 1, wherein said transactivation domain is selected from the group consisting of a Group H nuclear receptor member transactivation domain, a steroid/thyroid hormone nuclear receptor transactivation domain, a polyglutamine transactivation domain, a basic or acidic amino acid transactivation domain, a VP16 transactivation domain, a GAL4 transactivation domain, an NF-KB transactivation domain, a BP64 transactivation domain, a B42 acidic transactivation domain, and a p65 transactivation domain.

60. (Currently Amended) The virus of claim 3, wherein said virus is an adenovirus, adeno-associated virus, or retrovirus.

61. (Previously Presented) The vector of claim 50, wherein said vector is a plasmid.

62. (Previously Presented) The vector of claim 50, wherein said vector is an expression vector.

63. (Previously Presented) The vector of claim 50, wherein said vector is a viral vector.

64. (Currently Amended) The vector of claim 63, wherein said vector is an adenovirus vector, adeno-associated virus, or retrovirus.

65. (Previously Presented) The isolated host cell of claim 4, wherein said cell is a mammalian cell.

66. (Previously Presented) The isolated host cell of claim 65, wherein said mammalian cell is selected from the group consisting of a hamster cell, a murine cell, a monkey cell, a mouse cell, a rat cell, a rabbit cell, a cat cell, a dog cell, a bovine cell, a goat cell, a pig cell, a horse cell, a sheep cell, a monkey cell and a chimpanzee cell.

67. (Previously Presented) The isolated host cell of claim 4, wherein the host cell is selected from the group consisting of an *Aspergillus* cell, a *Trichoderma* cell, a *Saccharomyces* cell, a *Pichia* cell, a *Candida* cell, and a *Hansenula* cell.

68. (Previously Presented) The isolated host cell of claim 4, wherein the host cell is selected from the group consisting of a *Synechocystis* cell, a *Synechococcus* cell, a *Salmonella* cell, a *Bacillus* cell, an *Acinetobacter* cell, a *Rhodococcus* cell, a *Streptomyces* cell, an *Escherichia* cell, a *Pseudomonas* cell, a *Methylobacter* cell, an *Alcaligenes* cell, a *Synechocystis* cell, an *Anabaena* cell, a *Thiobacillus* cell, a *Methanobacterium* cell and a *Klebsiella* cell.

69. (Previously Presented) The isolated host cell of claim 4, wherein the host cell is a plant cell.

70. (Previously Presented) The isolated host cell of claim 69, wherein the plant cell is selected from the group consisting of an apple cell, an *Arabidopsis* cell, a bajra cell, a banana cell, a barley cell, a bean cell, a beet cell, a blackgram cell, a chickpea cell, a chili cell, a cucumber cell, an eggplant cell, a favabean cell, a maize cell, a melon cell, a millet cell, a mungbean cell, an oat cell, an okra cell, a *Panicum* cell, a papaya cell, a peanut cell, a pea cell, a pepper cell, a pigeonpea cell, a pineapple cell, a *Phaseolus* cell, a potato cell, a pumpkin cell, a rice cell, a sorghum cell, a soybean cell, a squash cell, a sugarcane cell, a sugarbeet cell, a sunflower cell, a sweet potato cell, a tea cell, a tomato cell, a tobacco cell, a watermelon cell, and a wheat cell.



71. (New) The multiple inducible gene modulation system of claim 9, wherein said nuclear receptor ligand binding domain is selected from the group consisting of a vertebrate retinoid X receptor ligand binding domain; an invertebrate retinoid X receptor ligand binding domain; an ultraspiracle protein ligand binding domain; and a chimeric ligand binding domain comprising two polypeptide **fragments**, wherein the first polypeptide fragment is from a vertebrate retinoid X receptor ligand binding domain, an invertebrate retinoid X receptor ligand binding domain, or an ultraspiracle protein ligand binding domain, and the second polypeptide fragment is from a different vertebrate retinoid X receptor ligand binding domain, invertebrate retinoid X receptor ligand binding domain, and an ultraspiracle protein ligand binding domain.

72. (New) The multiple inducible gene modulation system of claim 9, wherein said ecdysone receptor ligand binding domain is selected from the group consisting of a Lepidopteran ecdysone receptor ligand binding domain, a Dipteran ecdysone **receptor ligand** binding domain, an Arthropod ecdysone receptor ligand binding domain, an Orthopteran ecdysone receptor ligand binding domain, a Homopteran ecdysone receptor ligand binding domain, a Hemipteran ecdysone receptor ligand binding domain, a spruce budworm *Choristoneura fumiferana* ecdysone receptor ligand binding domain, a yellow meal worm *Tenebrio molitor* ecdysone receptor ligand binding domain, a tobacco hornworm *Manduca sexta* ecdysone receptor ligand binding domain, a tobacco budworm *Heliothis virescens* ecdysone receptor ligand binding domain, a goliard Chironomus tentans ecdysone receptor ligand binding domain, a silkworm *Bombyx mori* ecdysone

receptor ligand binding domain, a squinting bush brown *Bicyclus anynana* ecdysone receptor ligand binding domain, a buckeye *Junonia coenia* ecdysone receptor ligand binding domain, a fruit fly *Drosophila melanogaster* ecdysone receptor ligand binding domain, a yellow fever mosquito *Aedes aegypti* ecdysone receptor ligand binding domain, a blowfly *Lucilia capitata* ecdysone receptor ligand binding domain, a sheep blowfly *Lucilia cuprina* ecdysone receptor ligand binding domain, a blowfly *Calliphora vicina* ecdysone receptor ligand binding domain, a Mediterranean fruit fly *Ceratitis capitata* ecdysone receptor ligand binding domain, a locust *Locusta migratoria* ecdysone receptor ligand binding domain, an aphid *Myzus persicae* ecdysone receptor ligand binding domain, a fiddler crab *Celuca pugilator* ecdysone receptor ligand binding domain, an ixodid tick *Amblyomma americanum* ecdysone receptor ligand binding domain, and a white fly *Banecia argentifoli* ecdysone receptor ligand binding domain.

73. (New) The multiple inducible gene modulation system of claim 72, wherein said ecdysone receptor ligand binding domain is a spruce budworm *Choristoneura fumiferana* ecdysone receptor ligand binding domain.

74. (New) The multiple inducible gene modulation system of claim 9, wherein said DNA binding domain is selected from the group consisting of a GAL4 DNA binding domain, a LexA DNA binding domain, a transcription factor DNA binding domain, a Group H nuclear receptor member DNA binding domain, a steroid/thyroid hormone nuclear receptor superfamily member DNA binding domain, a bacterial LacZ DNA binding domain, DNA binding domain, and an ecdysone receptor DNA binding domain.

75. (New) The multiple inducible gene modulation system of claim 9, wherein said transactivation domain is selected from the group consisting of a Group H nuclear receptor member transactivation domain, a steroid/thyroid hormone nuclear receptor transactivation domain, a polyglutamine transactivation domain, a basic or acidic amino acid transactivation domain, a VP16 transactivation domain, a GAL4 transactivation domain, an NF-KB transactivation domain, a BP64 transactivation domain, a B42 acidic transactivation domain, and a p65 transactivation domain.